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RARE CASE OF TYPE II GLYCOGEN STORAGE DISEASE

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АБСТРАКТ

The article presents information about a rare case of Pompe disease. It is a glycogen storage disease. Pompe disease is a rare autosomal recessive disorder caused by deficiency of acid α -glucosidase (acid maltase deficiency). The defect of this enzyme leads to the accumulation of glycogen in the lysosomes of various tissues, with the development of the most pronounced changes in the skeletal muscles, myocardium and liver. During the third screening of a pregnant woman, the ultrasonography of the fetus's heart revealed the myocardial hypertrophy of the left ventricle perceived as posthypoxic. After delivery, the newborn underwent the ultrasound examination and molecular genetic studies. Firstly, the hepatomegaly and cardiomegaly were diagnosed. Then an infantile form of Pompe disease was found. The patient got enzyme replacement therapy without positive result. The death occurred at the age of 2 years and 5 months as a result of cardiovascular disease failure. Macroscopically, the sizes of the internal organs were increased. The microscopic examination demonstrated glycogen deposition in the myocardium, skeletal muscles, mucous membranes of the organs of the gastrointestinal tract, liver, kidney, spleen and adrenal glands.

Keywords: cardiomegaly; type II glycogenosis; glycogen storage disease; Pompe disease.

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АННОТАЦИЯ

В статье представлены данные о редкой форме болезней накопления II типа – болезни Помпе. Болезнь Помпе – это редкое аутосомно-рецессивное заболевание, вызванное врожденной недостаточностью кислой α -глюкозидазы (кислой мальтазы). Дефект этого фермента приводит к накоплению неметаболизированного гликогена в лизосомах различных органов и тканей, с развитием наиболее выраженных изменений в скелетных мышцах, миокарде и печени. Во время 3 планового скрининга беременной женщины при УЗИ сердца плода была диагностирована гипертрофия миокарда левого желудочка, расцененная как постгипоксическая. У новорожденного были диагностированы гепатомегалия и кардиомегалия. После молекулярно-генетического исследования выставлен диагноз инфантильной формы болезни Помпе. Проводилась ферментозамещающая терапия препаратом «Муозуте», однако заболевание прогрессировало, смерть наступила в возрасте 2-х лет и 5-ти месяцев от сердечно-сосудистой недостаточности. Макроскопически отмечалось увеличение внутренних органов в размерах. При микроскопическом исследовании выявлены обширные отложения гликогена в миокарде, скелетных мышцах, слизистых оболочках полых органов, печени, почках, селезенке, артериях и надпочечниках.

Ключевые слова: гликогеноз II типа; болезнь Помпе; кардиомегалия.

The article presents some information about a rare case of Pompe disease. Pompe disease is a rare autosomal recessive disorder caused by deficiency of acid α -glucosidase (acid maltase deficiency). It is glycogen storage disease.

The infantile form is characterized by acute course (duration). It manifests itself and leads to the death during the first year of life. The most frequent causes of death include pulmonary infections and cardiovascular failure.

The second (latest) form of the disease starts at the adolescent age. It is characterized by the absence of severe heart lesions and relatively positive prognosis. The major symptoms are the lesions of skeletal muscles. Death is caused by pulmonary failure [4].

Like many other rare genetic diseases, the data about the incidence of Pompe disease greatly differs from 1:14000 to 1:300000 [2], the infantile form being typical for Afro-Americans, South China and Taiwan, while the latent form – for Holland. Total incidence of the Pompe disease is 1:400000 [1, 3].

The clinical case under study is of great interest due to its rarity and, as a result, the absence of thorough description of pathological changes in different organs and tissues.

A Clinical case

The baby-girl was born from the second full term pregnancy in the incest marriage, with her parents being cousins. The body weight was 3430 grammes. The pregnancy was characterized by the chronic fetoplacental deficiency and intrauterine chronic hypoxia. During the third planned screening, the myocardial hypertrophy was found, which was confined after he birth.

Two weeks later, the examination showed the myocardial hypertrophy increasing (right ventricle – 5.2 mm, interatrial septum – 5.7, posterior wall of the left ventricle – 8 mm). When the baby was 4 weeks old, the interatrial septum became 12 mm, and the posterior wall of the left ventricle – 9 mm. The baby had a bad suckling, frequent possetting (regurgitation), tiredness, weakness, and gained no weight. The medical therapy had no result.

At the age of 3 months, in Moscow, the molecular genetic method revealed Pompe

disease. The girl underwent enzyme therapy with Myozyme with hardly any results.

When she was 2.1 years old, she suffered food aspiration followed by running temperature. The diagnosis of pneumonia was not confirmed, but the antibacterial therapy was performed with the small effect. On the third day, the patient was given artificial pulmonary ventilation due to increasing respiratory failure. On the fourth day, tracheostomy was performed. In spite of the therapy the state was worsening and the patient died on the 75 day after admission to hospital.

During the morphological examination, the deformation of the left part of the thorax was revealed (in the IV-V intercostal space on the midclavicular line). The heart was enlarged, ball-like, occupied the greatest part of the anterior mediastinum, weighed 120 grammes. The myocardium of the right ventricle was 0.5 cm (N-0.25). The left ventricle was very hypertrophic, its cavity was narrow and small, the myocardium was 3.0 cm (N-0.79). The papillary muscles were very thick, chordate tendineae were shortened. The perimeter of the mitral valve was 45 mm. The endocardium of the left atrium was whitened and thickened up to 1.0 mm. On cutting the myocardium, it was dim and red-brown, with scattered whitened spots 0.3-0.5 cm in size. The interventricular septum was 1.5 cm.

The microscopically large areas of the cardiomyocytes with glycogen deposits are seen (Fig. 1). The nuclei are small and removed to the peripheral part of cells. The relatively normal cardiomyocytes are rare, hypertrophic with bright eosinophilic cytoplasm containing light big vacuoles. Their nuclei are deformed, different in form and size, located peripherally. The coronary arteries are narrowed with evident sclerotic changes. In some parts of the left ventricle, some small areas of fibrosis with full blood capillaries surrounded by hypertrophic cardiomyocytes are found. Occasional ischemic and necrobiotic lesions of cardiomyocytes without clearly seen cells reaction were identified (Fig. 2).

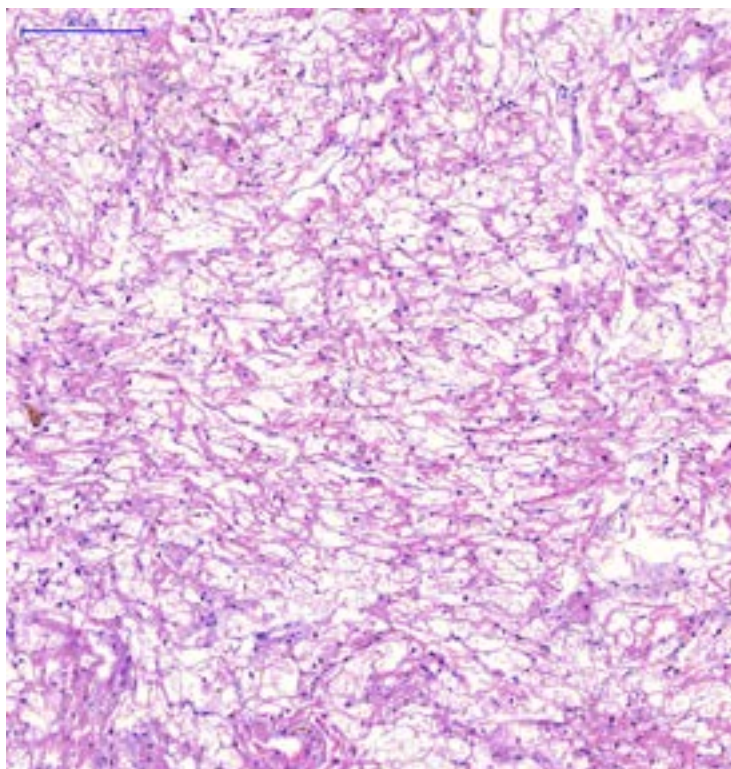


Рисунок 1. Диффузные отложения гликогена в кардиомиоцитах.

Окр. гематоксилин+эозин. Ув. $\times 100$.

Figure 1. Diffuse glycogen deposits in cardiomyocytes (H&E stain, $\times 100$).

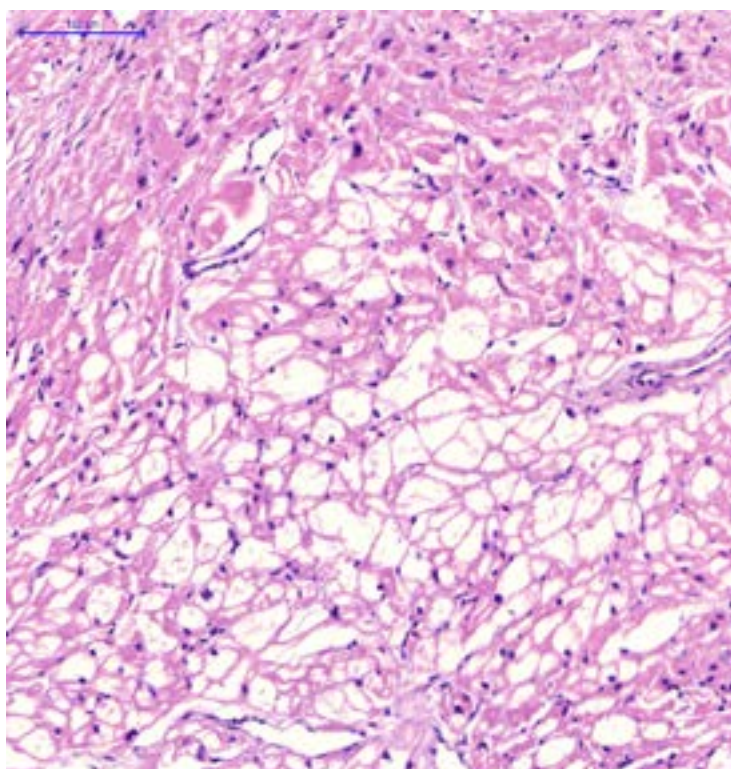


Рисунок 2. Отложения гликогена в кардиомиоцитах. Очаговый мелкоочаговый кардиосклероз. Атрофические-гипертрофические изменения кардиомиоцитов.

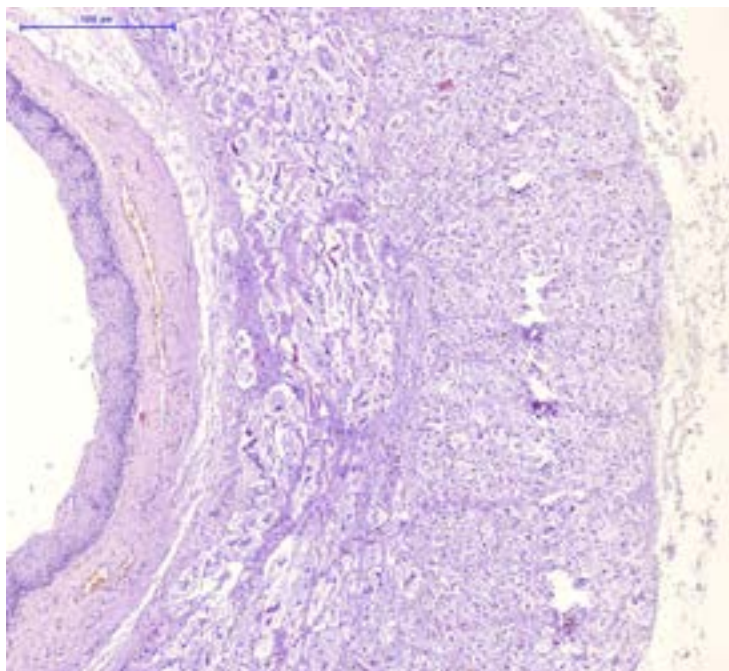
Окр. гематоксилин+эозин. Ув. $\times 200$.

Figure 2. Diffuse glycogen deposits in cardiomyocytes. Local cardiosclerosis. Atrophic and hypertrophic changes of the cardiac muscle (H&E stain, $\times 200$).

No evident signs of lesions in other organs were discovered, except a severe edema of the mucous membrane of the gastrointestinal tract and the respiratory system. However, in histological examination, there were found total diffuse deposits of glycogen in the cell cytoplasm of the muscular coat of the pharynx and esophagus, as well as in the skeletal muscles, surrounding the salivary glands, in those of pelvis, tongue, and diaphragm (Fig. 3). Clinically

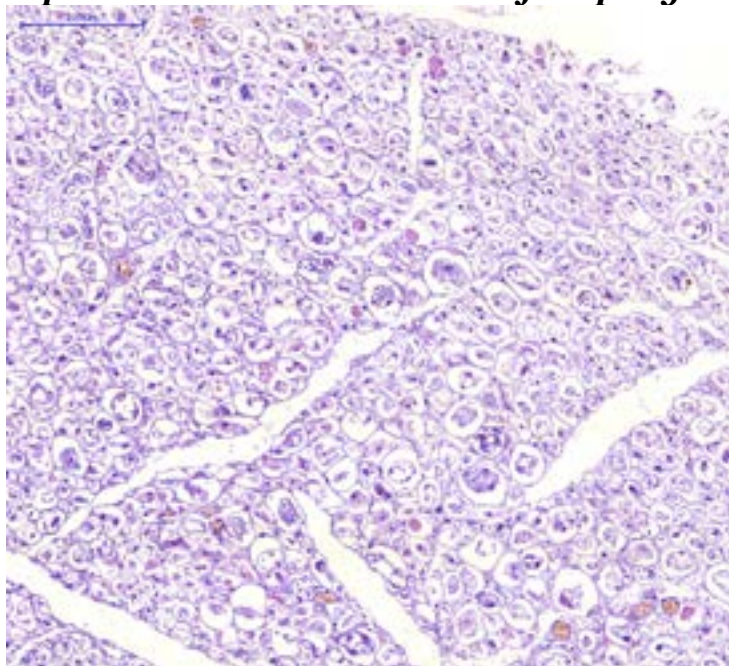
these signs showed themselves in swallow disturbance, breathing and muscle weakness.

Diffuse glycogen deposits were found in zona glomeruloza and zona fasciculate of the suprarenal cortex. The liver was flabby and red-brown in color. Microscopically, the normal histological structure of the liver was not found. The cytoplasm of hepatocytes was filled with the deposits of glycogen (Fig. 4). The nuclei themselves were small and atrophic.



**Рисунок 3. Отложения гликогена в мышечной оболочке пищевода.
Окр. гематоксилин+эозин. Ув. ×100.**

Figure 3. Glycogen deposits in the muscular coat of esophagus (H&E stain, ×100).



**Рисунок 4. Диффузные отложения гликогена в миоцитах скелетных мышц. Окр.
гематоксилин+эозин. Ув. ×100.**

Figure 4. Diffuse glycogen deposits in the skeletal muscle (H&E stain, ×100).

The microscopic examination revealed evident dilatation of capillaries and arteries of small diameter with thickened walls. On separate spots, there was diapedesis around capillaries. Inter-alveolar septa of lungs were full blooded, some of them were thin and broken. Macrophages, leucocytes and pale-pink substance were seen in the alveoli.

Diagnosis. Glycogenosis of Type II, infantile form with diffusive glycogen deposits in the heart, suprarenal gland, tongue, esophagus, diaphragm, and skeletal muscles.

Complications. Cardiomegaly, left and right ventricle hypertrophy with multiple areas of car-

diosclerosis, ischemia, subendocardial necrosis. Lungs hypertension: thickening of the lungs vessels, perivascular diapedesis, pulmonary edema. Wave-like degeneration of cardiomyocytes. Microfocal pneumonia. General neonatal hypotrophy.

Accompanying diseases. Hypoplasia of the suprarenal gland, thymus, and spleen. Microfocal productive sialoadenitis.

Thus, the 2.5 year old patient had Type II glycogenosis (Pompe disease) followed by heart, skeletal muscles, and internal organ lesion, which caused the heart failure and arrhythmias asystolia and finally death.

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